

Mating Scheme For Production Of HbA Replacement Mice

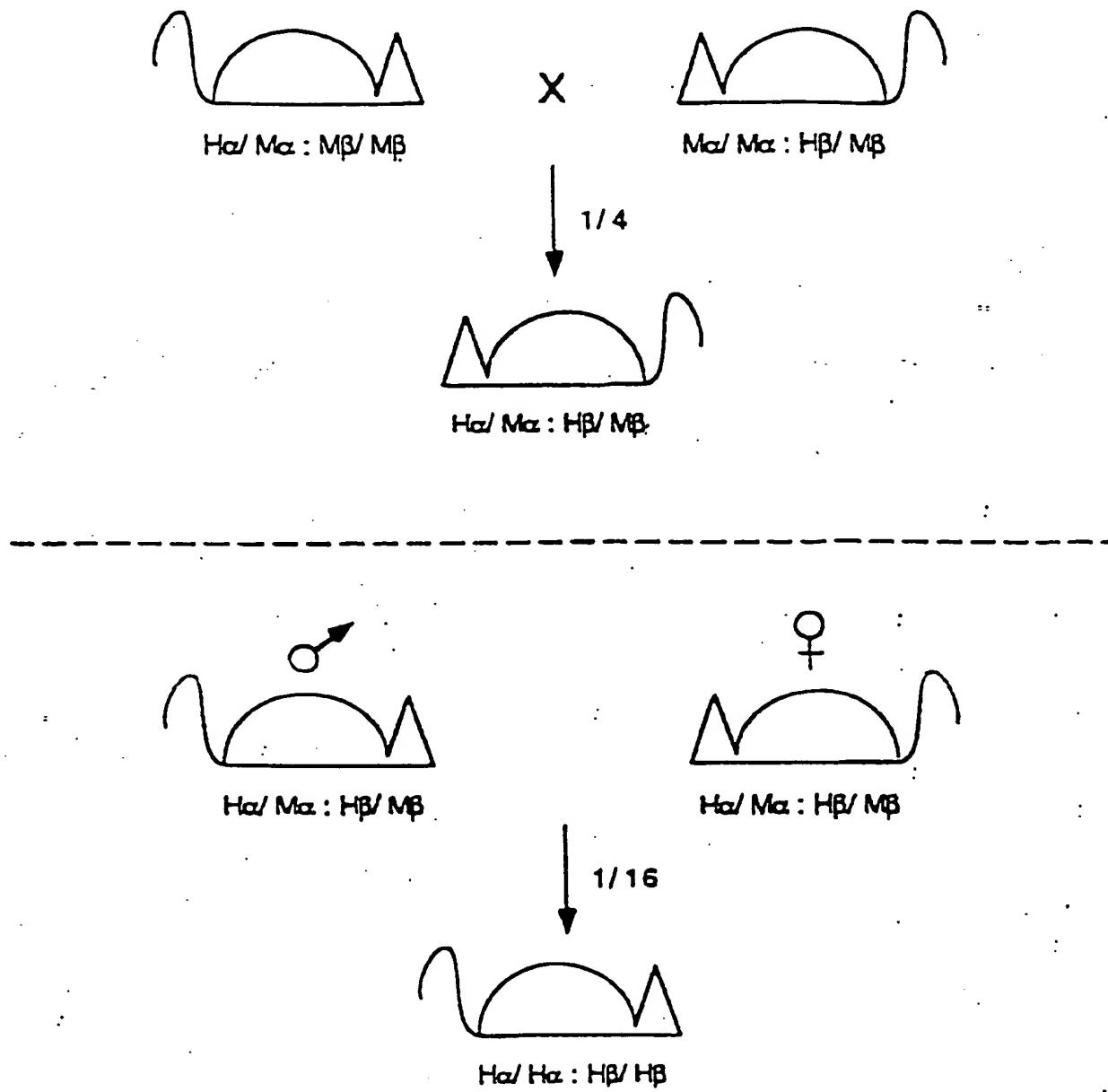
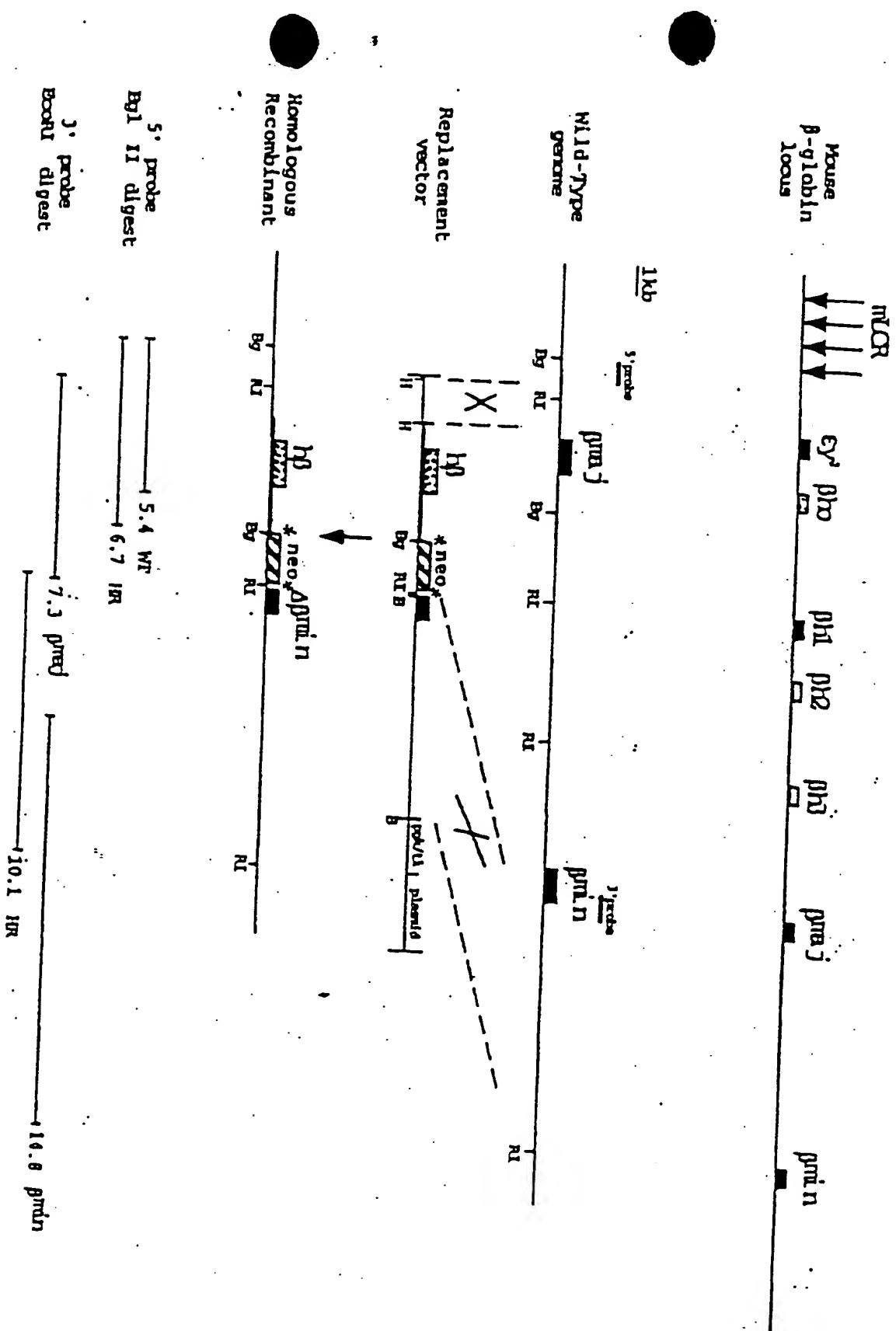


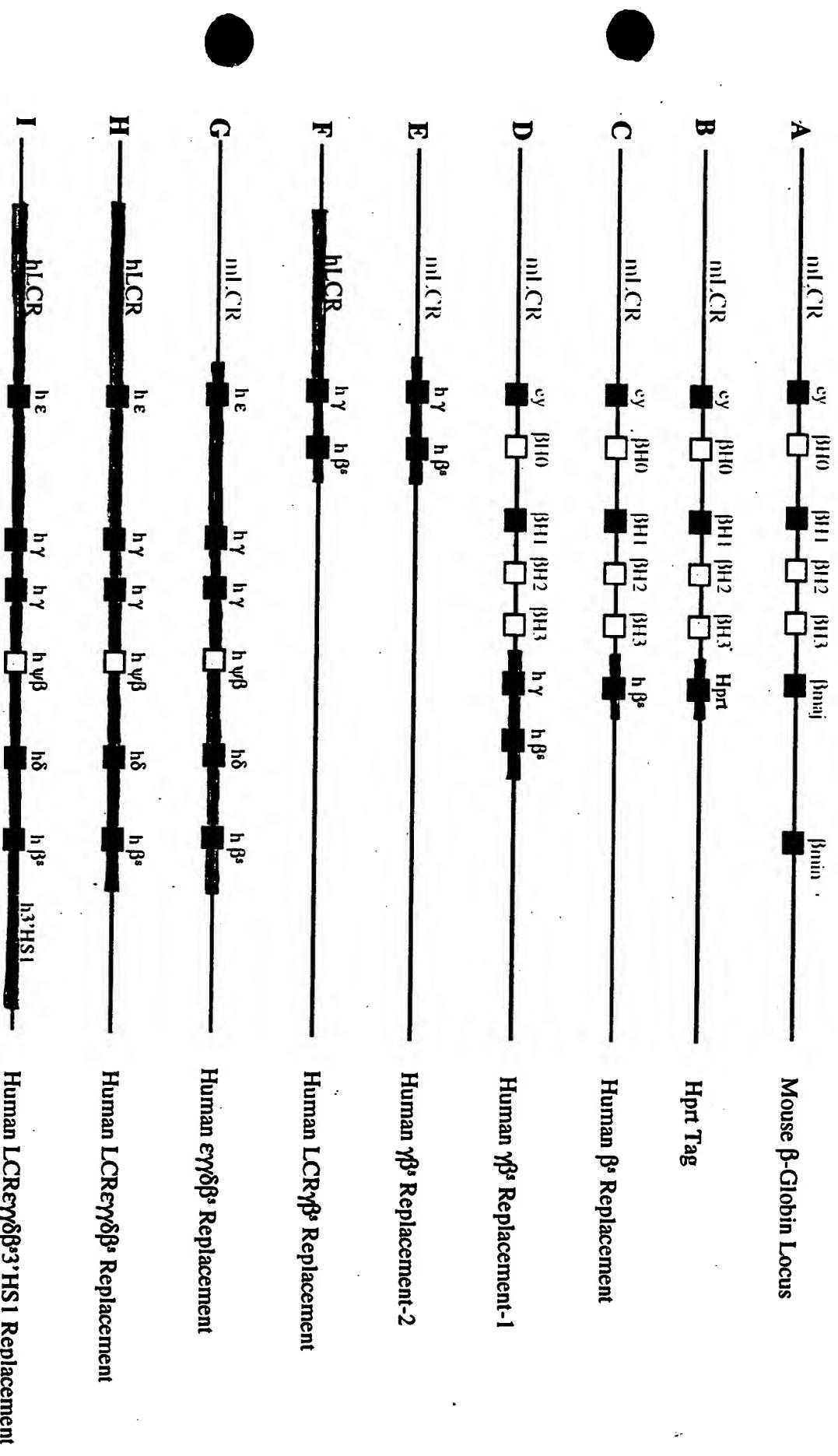
FIG. 1

FIG. 2

Mouse β KO/human β replacement



Human Replacement Of The Mouse β -Globin Locus



Human Replacement Of The Mouse α -Globin Locus

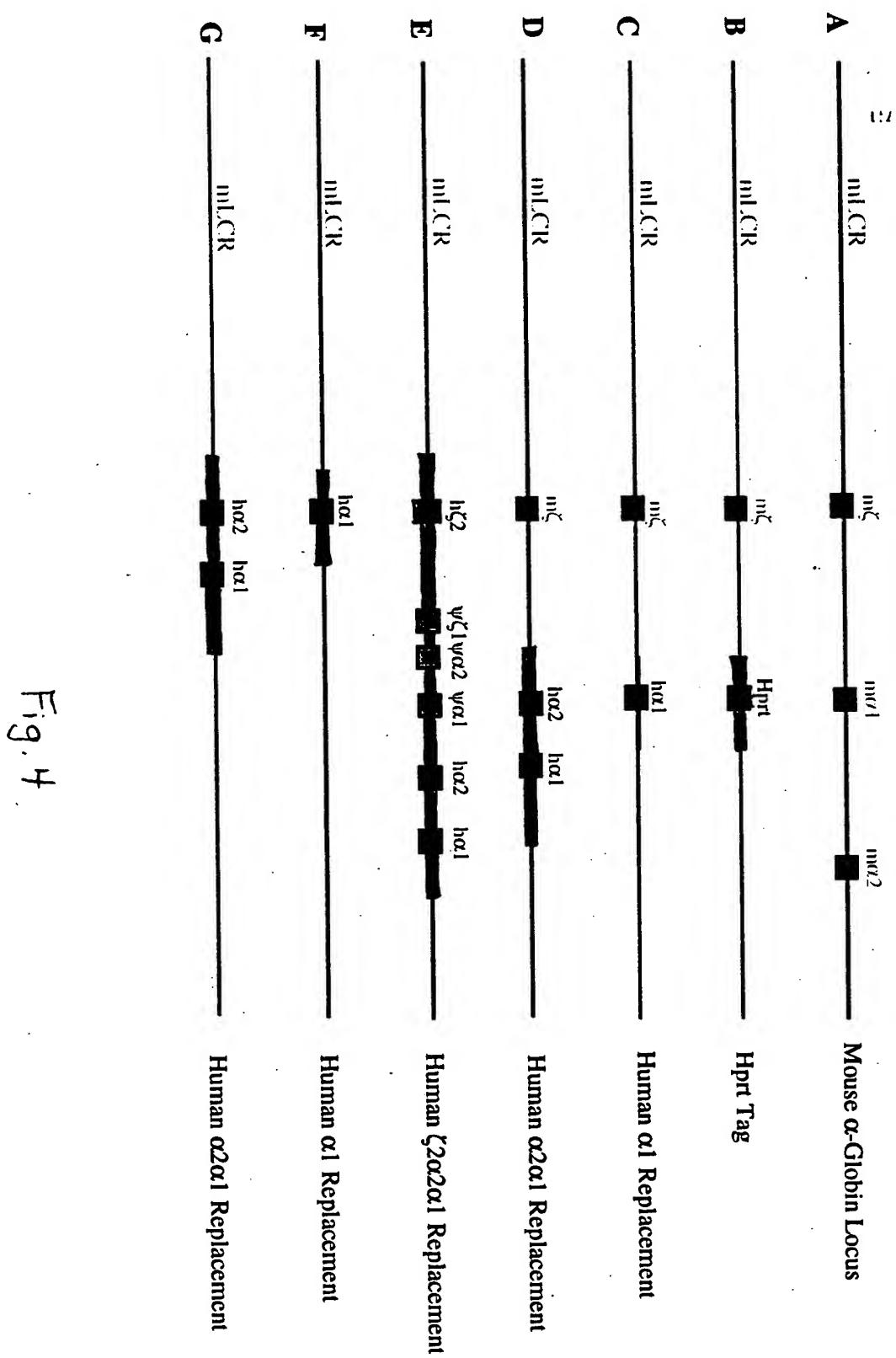


Fig. 4

Production Of Transgenic HbF → HbA Mice
(Doubly Homozygous For Mouse α -Globin And β -Globin Deletions)

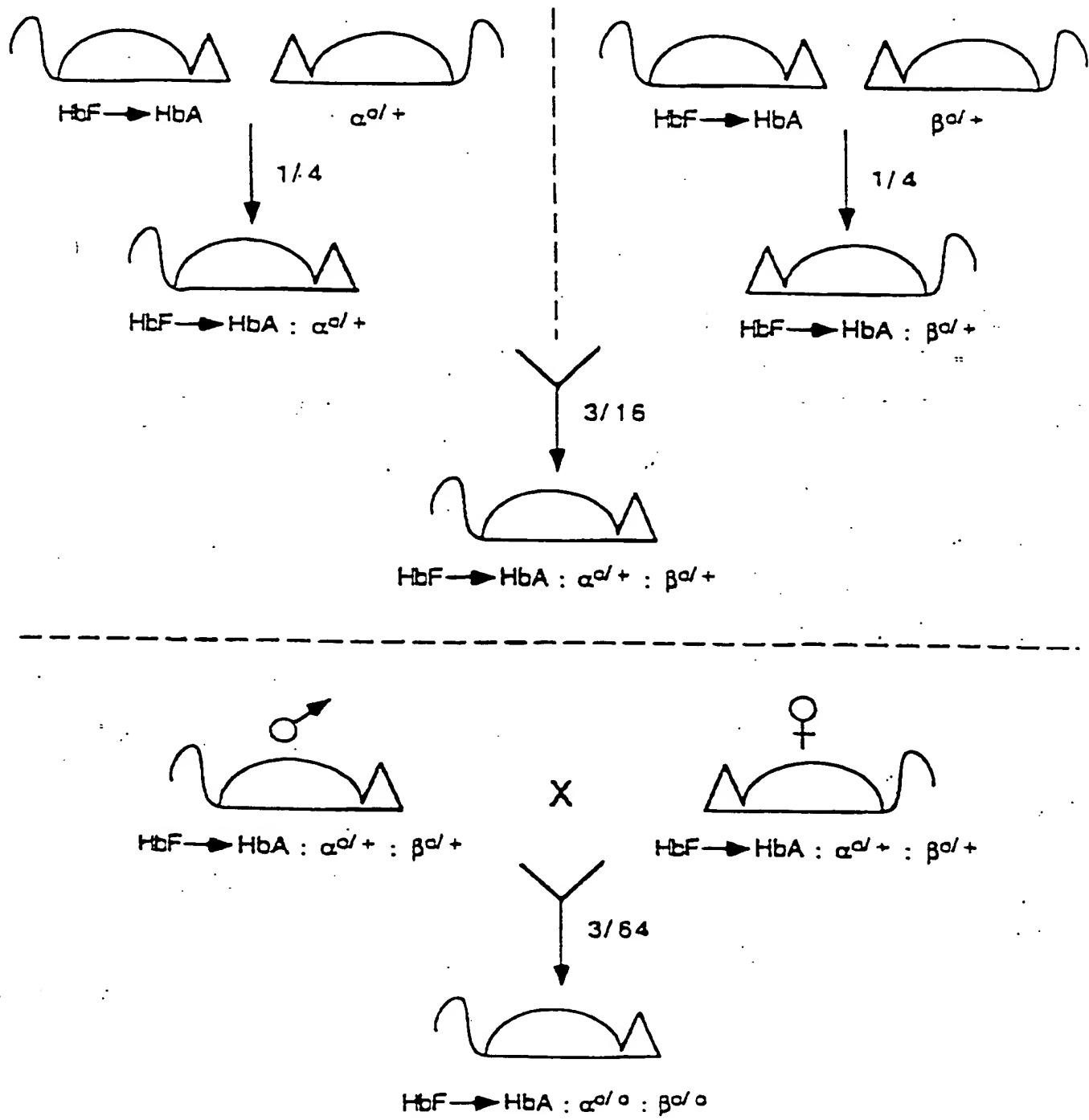
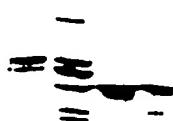


FIG. 5

Isoelectric Focusing Gel Of Transgenic Mouse Hemolysates

1 2 3 4

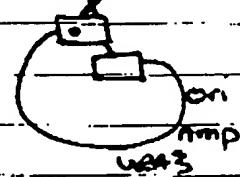
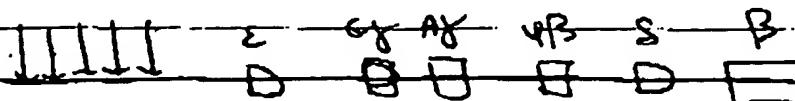


1. Mouse Control
2. $\text{HbF} \rightarrow \text{HbA} : \alpha^{+/+} : \beta^{+/+}$ Mouse
3. $\text{HbF} \rightarrow \text{HbA} : \alpha^{\alpha/\alpha} : \beta^{\alpha/\alpha}$ Mouse
4. Human AA Control

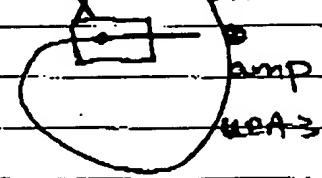
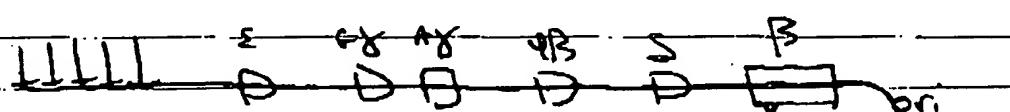
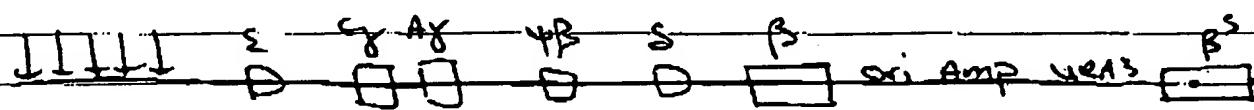
FIG. 6

FIG. 7

YAC



select for URA3⁺



select for URA3

(5-fluoro-orotic acid)

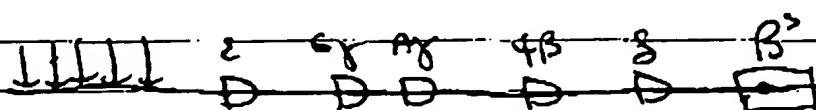
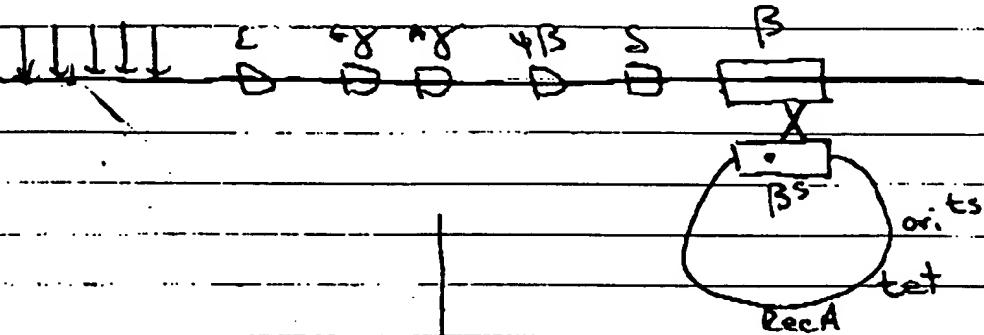
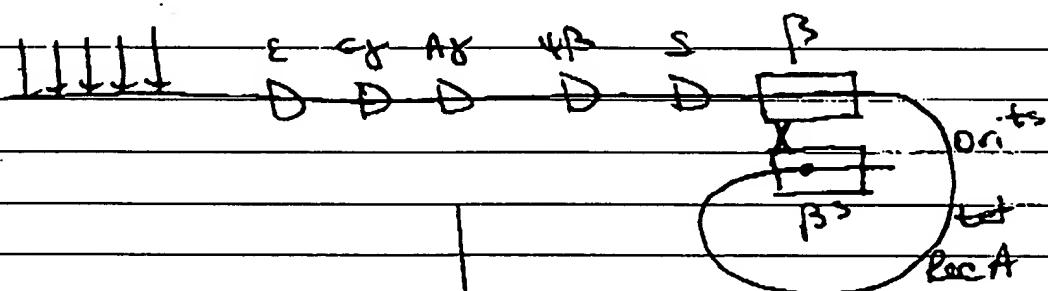
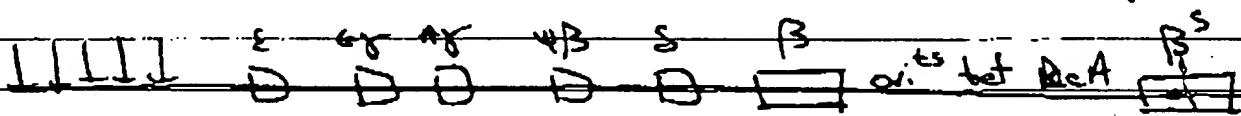


FIG. 8

BAC



select for tet^R at $43^\circ C$
(non-permissive temp for ori^ts)



select for tet^S (Fusaric Acid)
at $37^\circ C$

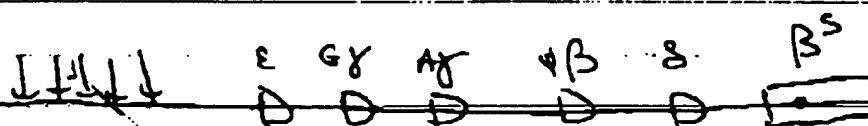


FIG. 9A

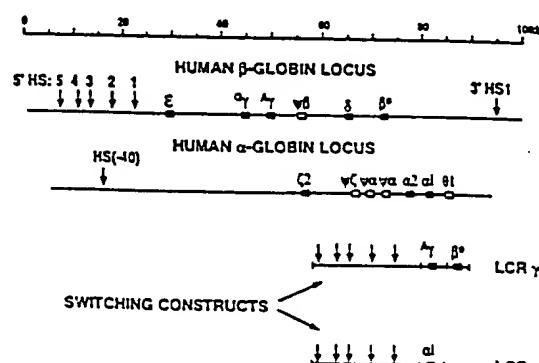


FIG. 9B

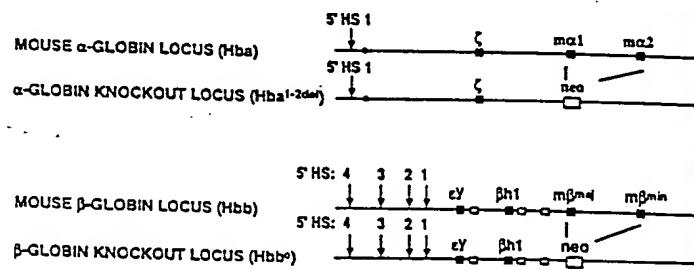
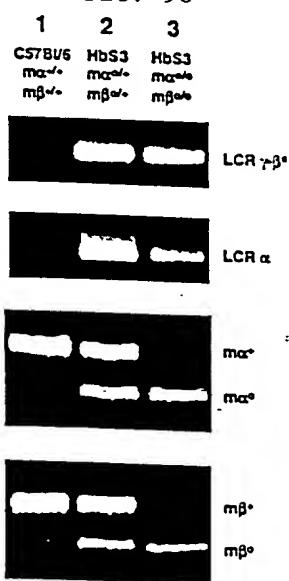


FIG. 9C



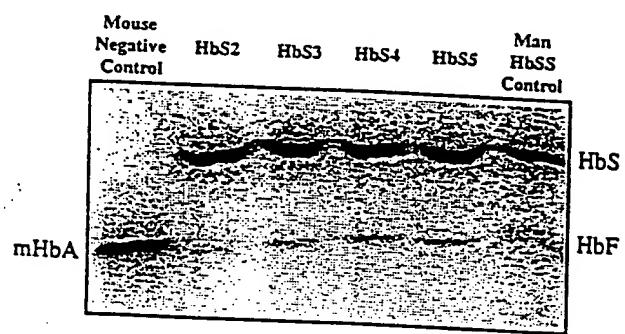


FIG. 10

FIG. 11A

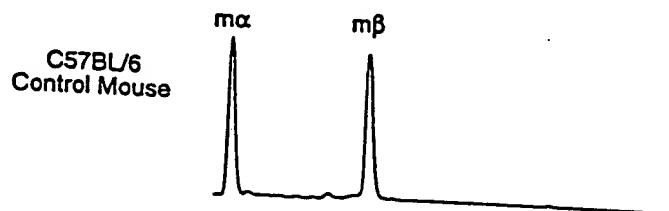


FIG. 11B

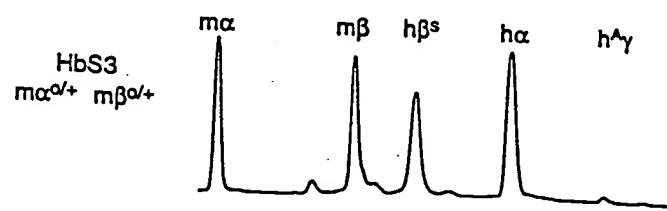


FIG. 11C

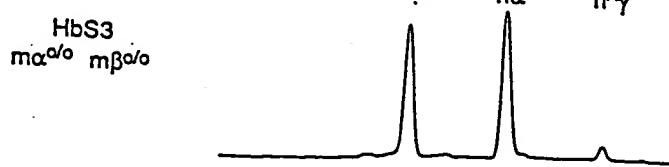
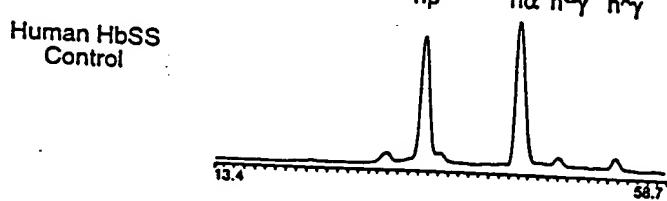


FIG. 11D



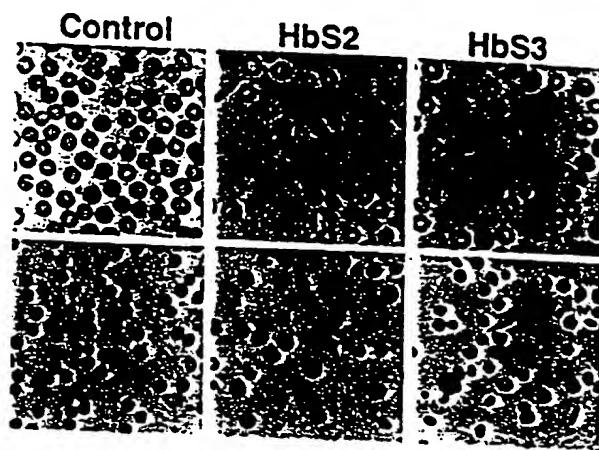


FIG. 12

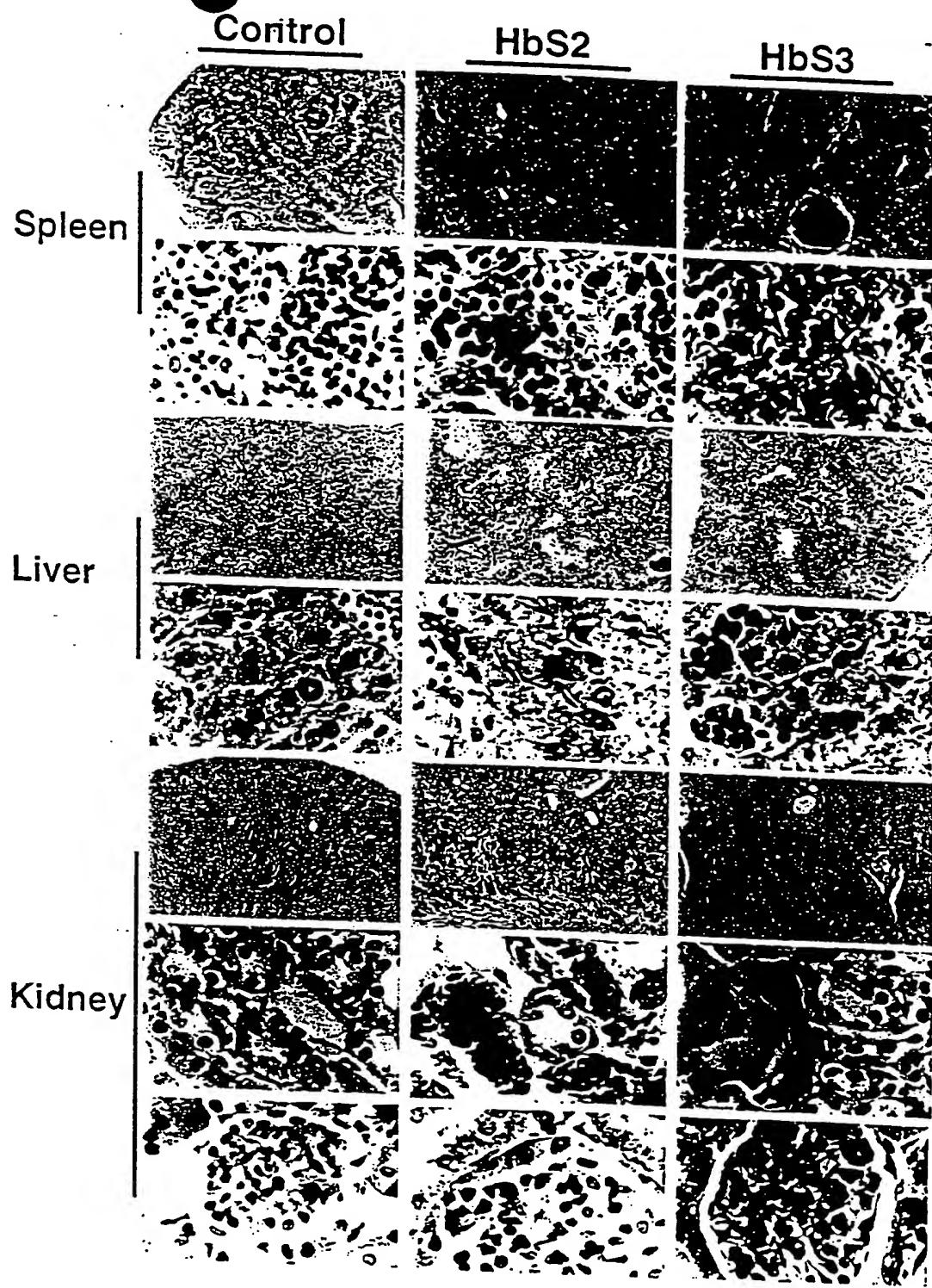


FIG. 13

FIG. 14A

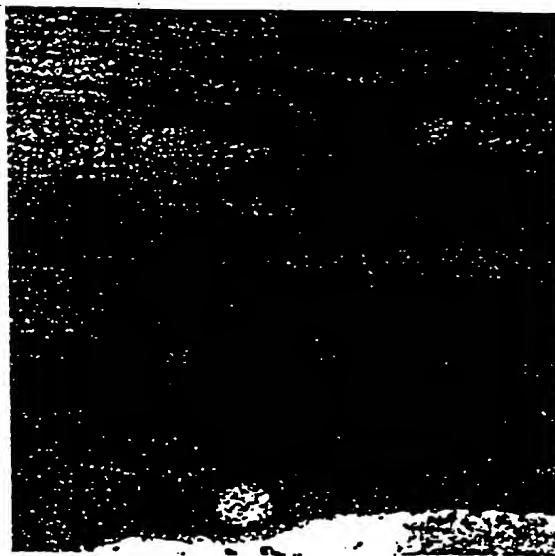


FIG. 14B



Hemoglobin Switching In HbA Mice

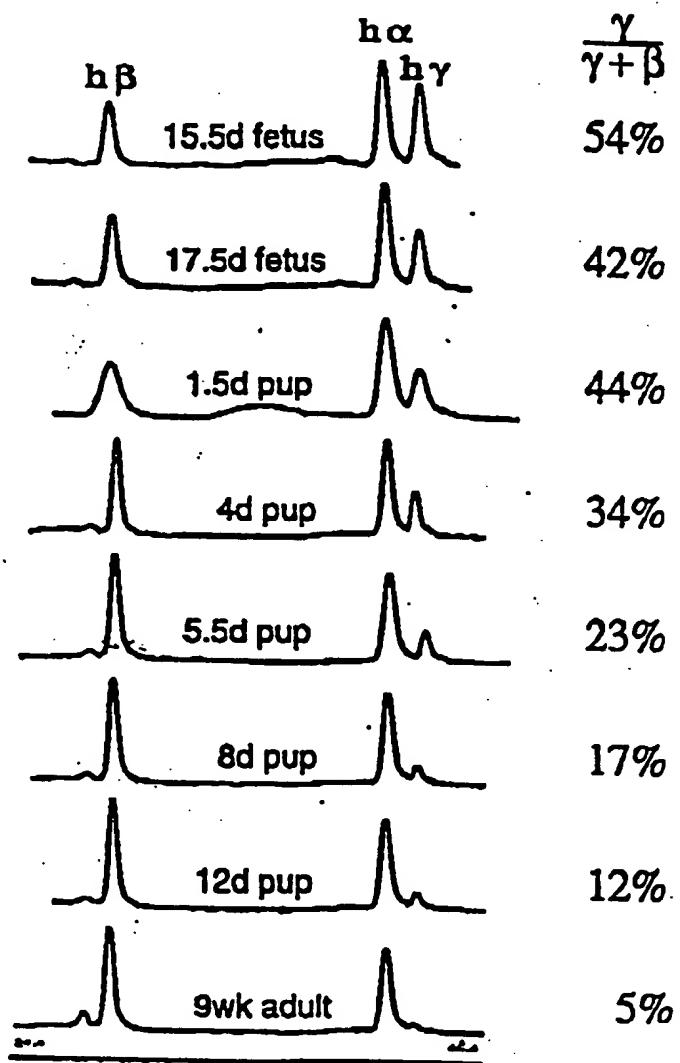


FIG. 15

Increasing HbF Levels In HbS Mice:
Crossing The HbS 3 and HbF Lines

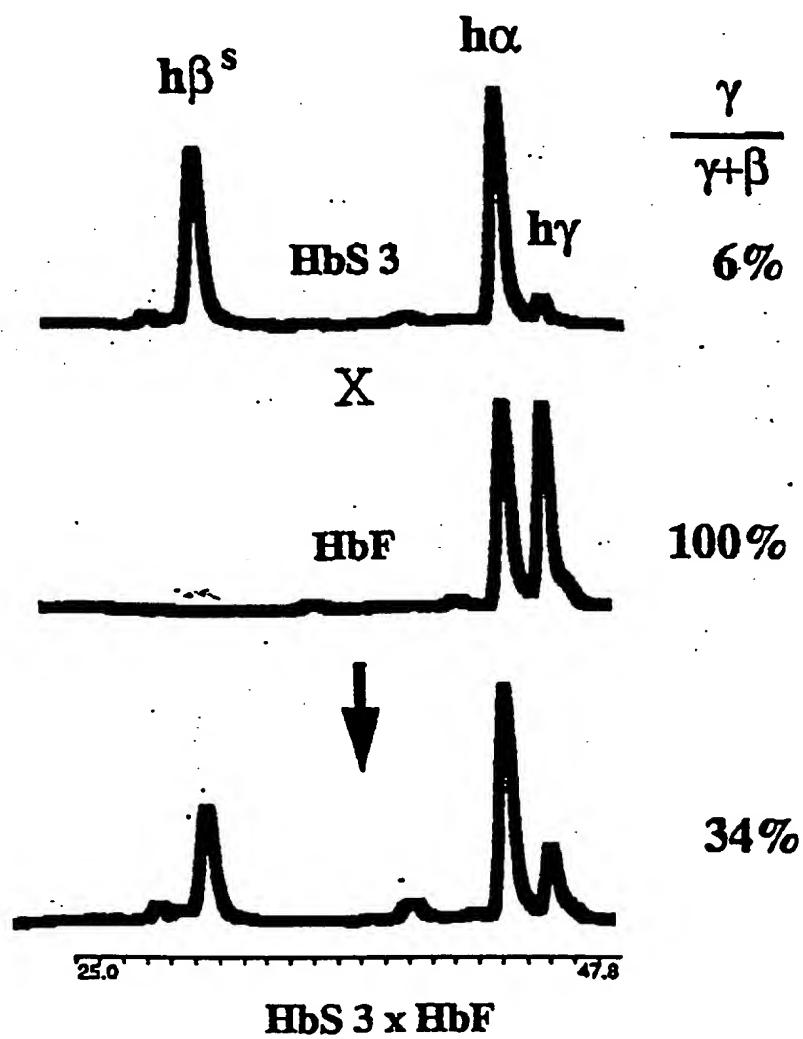


FIG. 16